

Amendment to the Claims:

This listing of the claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

Claim 1 (Currently amended): A method for determining binding of an ~~unknown~~ immunoglobulin to a target in an intracellular environment, comprising the steps of:

a) providing a first fusion polypeptide comprising an immunoglobulin fused to a first molecule, wherein said immunoglobulin was subjected to no more than one preselection step; and in an intracellular environment, a first molecule and a second molecule, wherein specific interaction of the first and second molecules leads to the generation of a signal, wherein an unknown immunoglobulin is associated with the first molecule, and wherein an intracellular target is associated with the second molecule, such that binding of the immunoglobulin to the target leads to the specific interaction of the first and second molecules and generation of the signal; and

b) providing a second fusion polypeptide comprising a target fused to a second molecule, wherein said first and second molecules are separable domains of a reporter molecule; and assessing the intracellular binding between the immunoglobulin and the target by monitoring the signal.

c) expressing said first fusion polypeptide together with said second fusion polypeptide in an intracellular environment, wherein binding of said immunoglobulin with said target brings said first molecule and said second molecule into operative association to produce a detectable reporter molecule, and

d) detecting said detectable reporter molecule, wherein said detection is indicative of binding between said immunoglobulin and said target in an intracellular environment.

Claim 2 (Canceled).

Claim 3 (Canceled).

Claim 4 (Currently amended): The method of claim 1 ~~3~~, wherein the ~~active~~ reporter molecule is selected from the group consisting of a transcription factor, an enzyme and a bioluminescent molecule.

Claim 5 (Currently amended): The method of claim 4 wherein the ~~active~~ reporter molecule is an enzyme and the method is performed in the presence of a substrate for the enzyme.

Claim 6 (Canceled).

Claim 7 (Currently amended): The method of claim 1 ~~6~~, wherein the first molecule is the activation domain of VP16 and the second molecule is the DNA-binding domain of LexA.

Claim 8 (Currently amended): The method of claim 1, wherein the ~~signal~~ detecting step is selected from the group consisting of a change in an optical property and the activation of a reporter gene.

Claim 9 (Currently amended): The method of claim 8, wherein the ~~signal~~ detecting step allows the sorting of cells.

Claim 10 (Previously presented): The method of claim 1, wherein the immunoglobulin is selected from the group consisting of an intact immunoglobulin, a Fv, a scFv, a Fab and a F(ab')₂.

Claim 11 (Previously presented): The method of claim 1, wherein the immunoglobulin is provided by expressing an immunoglobulin-encoding nucleic acid within the cell.

Claim 12 (Previously presented): The method of claim 11, wherein the immunoglobulin-encoding nucleic acid is obtained from a library of immunoglobulin-encoding nucleic acids.

Claim 13 (Previously presented): The method of claim 12, wherein the library is a phage library encoding a repertoire of immunoglobulins.

Claim 14 (Previously presented): The method of claim 12, wherein the library is constructed from nucleic acids isolated from an organism which has been challenged with an antigen.

Claim 15 (Previously presented): The method of claim 1, comprising the further step of:

e) isolating those immunoglobulins which give rise to a signal.

Claim 16 (Previously presented): The method of claim 15, comprising the further step of:

f) subjecting the selected immunoglobulins to a functional intracellular assay.

Claim 17 (Previously presented): The method of claim 1, wherein one or both of the immunoglobulin and the target, together with the first or second molecules, are provided in the form of nucleic acid constructs which are transcribed to produce said immunoglobulin and/or target together with said first or second molecules.

Claim 18 (Withdrawn): A method for preparing an immunoglobulin suitable for use in a procedure according to claim 1, comprising the steps of:

(a) expressing a repertoire of immunoglobulin genes in a selection system and isolating those genes which encode immunoglobulins specific for a desired target;

(b) bringing the isolated genes into operative association with nucleic acids encoding a first molecule, wherein stable interaction of the first molecule with a second molecule generates a signal, in order to produce a fusion polypeptide comprising the immunoglobulin and the first molecule.